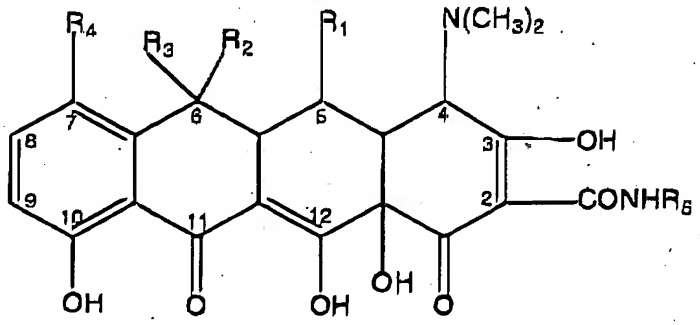
APPENDIX: Claims as pending in this application, marked to sh w amendments

1. (amended) A pharmaceutical composition comprising an effective amount of a poorly absorbed tetracycline in the form of a polyvalent metal ion complex in a carrier for topical administration wherein less than 10% of the tetracycline is absorbed into the systemic circulation when topically administered.

2. The composition of claim 1 wherein the tetracycline is selected based on poor oral absorption from the group consisting of tetracyclines defined by the following structure:



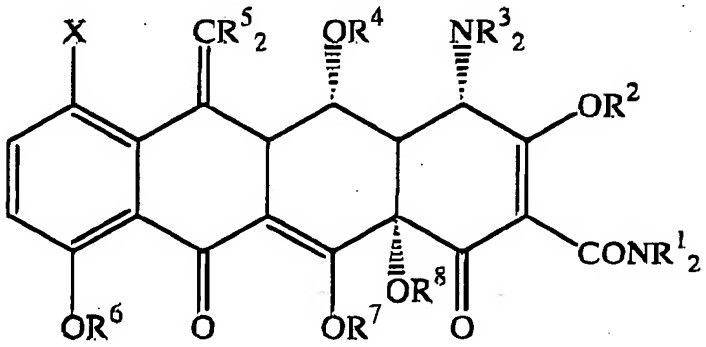
wherein R_1-R_5 may be a hydrogen atom, a halogen atom, a hydroxyl group, or any other organic composition comprising from 1-8 carbon atoms and optionally include a heteroatom such as nitrogen, oxygen, in linear, branched, or cyclic structural formats.

3. The composition of claim 2 wherein R_1 and R_2 are hydrogen or a hydroxyl group; R_3 is hydrogen or a methyl group; R_4 is a hydrogen atom, a halogen, or a nitrogen containing entity; and R_5 is a hydrogen atom, or nitrogen containing ring structure.

4. The composition of claim 2 wherein the tetracycline is modified by substitution of H at carbon 9 by a substituted amido group.

5. The composition of claim 2 wherein the tetracycline is modified at any of positions 1 through 4 and 10 through 12.

6. The composition of claim 2 having the following structure:



wherein R^1, R^2, R^3, R^4, R^5, R^6, R^7, and R^8 can be H, C1-C3 alkyl, phenyl, and aryl groups; and

wherein X is an H, alkyl, alkoxy, phenoxy, aryloxy, amino group, amide, acyl, and halo group; and pharmaceutically acceptable salts thereof.

7. The composition of claim 6 wherein R^1, R^2, R^4, R^5, R^6, R^7, and R^8 are H; wherein R^3 is CH_3; and wherein X is a chloro group.

8. The composition of claim 1 wherein the carrier for topical administration to the mucosa of the oral cavity and gastro-intestinal tract is selected from the group consisting of a mouthwash, lozenge, tablet, paste and gel.

9. The composition of claim 1 wherein the carrier for topical administration comprises the tetracycline coated onto or encapsulated into a carrier selected from the group consisting of powders, pellets, microcapsules, liposomes, and emulsions.

10. The composition of claim 9 wherein the tetracycline is formulated as a dry powder.

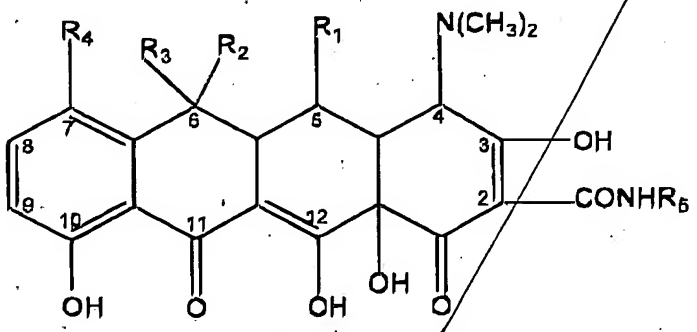
11. The composition of claim 1 wherein less than 10% of the tetracycline is absorbed into the systemic circulation when topically administered to the mouth and then swallowed.

13. (amended) The composition of claim [12] 1 wherein the polyvalent metal ion is calcium or magnesium.

14. The composition of claim 1 wherein the tetracycline is formulated to be topically administered to the mucosa as an aerosol.

15. (amended) A method for treating a patient in need thereof comprising administering to the patient an effective amount of a poorly absorbed tetracycline in the form of a polyvalent metal ion complex in a carrier for topical administration wherein less than 10% of the tetracycline is absorbed into the systemic circulation when topically administered.

16. The method of claim 15 wherein the tetracycline is selected based on poor absorption from the group consisting of tetracyclines defined by the following structure:



wherein R_1-R_5 may be a hydrogen atom, a halogen atom, a hydroxyl group, or any other organic composition comprising from 1-8 carbon atoms and optionally include a heteroatom such as nitrogen, oxygen, in linear, branched, or cyclic structural formats.

17. The method of claim 15 wherein the tetracycline is selected from the group consisting of compounds with the formula wherein R_1 and R_2 are hydrogen or a hydroxyl group; R_3 is hydrogen or a methyl group; R_4 is a hydrogen atom, a halogen, or a nitrogen containing entity and R_5 is a hydrogen atom, or nitrogen containing ring structure, compounds wherein the tetracycline is modified at any of positions 1 through 4 and 10 through 12, and compounds wherein the tetracycline is modified by substitution of H at carbon 9 by a substituted amido group.

18. The method of claim 16 wherein the tetracycline has the following structure:

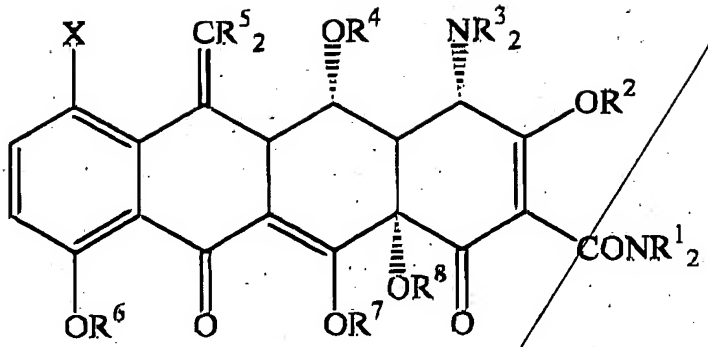
21. The method of claim 15 wherein the carrier for topical administration comprises the tetracycline coated onto or encapsulated into a carrier selected from the group consisting of powders, pellets, microcapsules, liposomes, and emulsions, comprising suspending or dissolving the tetracycline and carrier in a liquid for adminstration of the tetracycline to the patient.

22. The method of claim 15 wherein the tetracycline is administered daily starting at least one day before the patient is treated with radiation or chemotherapy.

23. The method of claim 15 wherein the patient is treated between one and six times daily.

24. (twice amended) A method for making a composition for treating a patient to prevent or treat mucositis comprising

[making a formulation for topical administration of] formulating an effective amount to prevent or treat mucositis of a tetracyline in the form of a polyvalent metal ion complex which has less than 10% bioavailability when orally adminstered in a carrier for topical administration to the mucosa.



wherein R^1, R^2, R^3, R^4, R^5, R^6, R^7, and R^8 can be H, C1-C3 alkyl, phenyl, and aryl groups; and wherein X is an H, alkyl, alkoxy, phenoxy, aryloxy, amino group, amide, acyl, and halo group; and pharmaceutically acceptable salts thereof.

19. The method of claim 18 wherein the tetracycline is meclocycline, wherein R^1, R^2, R^4, R^5, R^6, R^7, and R^8 are H;

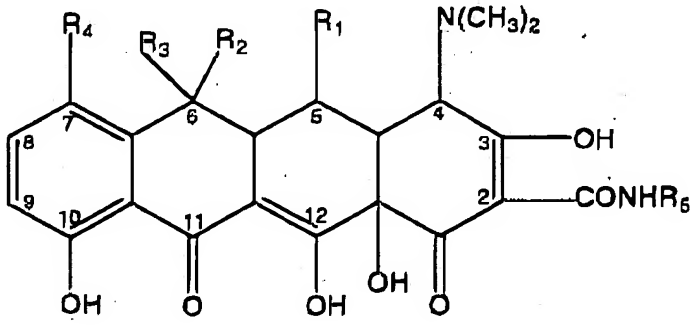
wherein R^3 is CH_3; and wherein X is a chloro group.

20. The method of claim 15 wherein the carrier for topical administration to the mucosa of the oral cavity and gastro-intestinal tract is selected from the group consisting of a mouthwash, lozenge, tablet, paste and gel.

U.S.S.N. 10/007,197
Filed: March 23, 2001
CLAIMS AS PENDING

APPENDIX: Claims as pending in U.S.S.N. 09/661,836

1. (Amended) A pharmaceutical composition for treating or preventing mucositis comprising as the sole active agents an effective amount of a poorly absorbed tetracycline defined by the following structure:



wherein R_1-R_5 may be a hydrogen atom, a halogen atom, a hydroxyl group, or any other organic composition comprising from 1-8 carbon atoms and optionally include a heteroatom such as nitrogen, oxygen, in linear, branched, or cyclic structural formats, alone or in combination with a compound selected from the group consisting of local anesthetics and antifungal agents, in a carrier for topical administration to the mucosa.

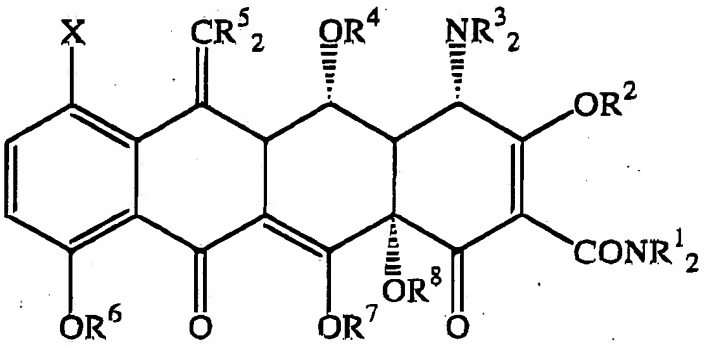
2. (Amended) The composition of claim 1 wherein the carrier for topical administration to the mucosa of the oral cavity and gastrointestinal tract is a mouthwash formulation.

3. (Amended) The composition of claim 1 wherein R_1 and R_2 are hydrogen or a hydroxyl group; R_3 is hydrogen or a methyl group; R_4 is a hydrogen atom, a halogen, or a nitrogen containing entity; and R_5 is a hydrogen atom, or nitrogen containing ring structure.

4. (Amended) The composition of claim 1 wherein the tetracycline is modified by substitution of H at carbon 9 by a substituted amido group.

5. (Amended) The composition of claim 1 wherein the tetracycline is modified at any of positions 1 through 4 and 10 through 12.

6. (Amended) The composition of claim 1 having the following structure:



wherein R^1, R^2, R^3, R^4, R^5, R^6, R^7, and R^8 can be H, C1-C3 alkyl, phenyl, and aryl groups; and

wherein X is an H, alkyl, alkoxy, phenoxy, aryloxy, amino group, amide, acyl, and halo group; and pharmaceutically acceptable salts thereof.

7. The composition of claim 6 wherein R^1, R^2, R^4, R^5, R^6, R^7, and R^8 are H; wherein R^3 is CH_3; and wherein X is a chloro group.

8. (Amended) The composition of claim 1 wherein the carrier for topical administration to the mucosa of the oral cavity and gastro-intestinal tract is selected from the group consisting of a lozenge, tablet, paste and gel.

9. The composition of claim 1 wherein the carrier for topical administration comprises the tetracycline coated onto or encapsulated into a carrier selected from the group consisting of powders, pellets, microcapsules, liposomes, and emulsions.

10. The composition of claim 9 wherein the tetracycline is formulated as a dry powder.

11. The composition of claim 1 wherein less than 10% of the tetracycline is absorbed into the systemic circulation when topically administered to the mouth and then swallowed.

12. (Amended) The composition of claim 1 wherein the tetracycline is in the form of a polyvalent metal ion complex.

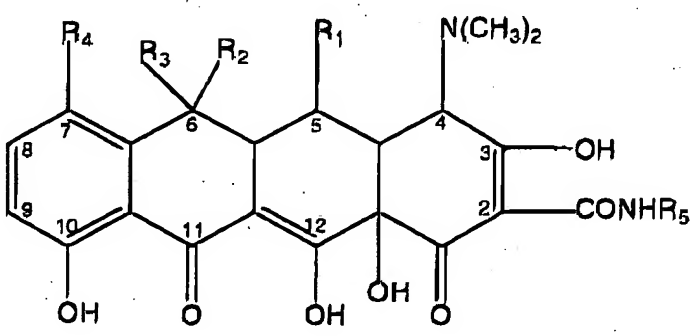
13. The composition of claim 12 wherein the polyvalent metal ion is calcium or magnesium.

14. The composition of claim 1 wherein the tetracycline is formulated to be topically administered to the mucosa as an aerosol.

APPENDIX - Claims as Pending in U.S.S.N. 09/815,762

15. (amended) A method for treating a patient in need thereof comprising administering to the patient an effective amount of a poorly absorbed tetracycline in a carrier for topical administration to the mucosa to treat mucositis.

16. The method of claim 15 wherein the tetracycline is selected based on poor absorption from the group consisting of tetracyclines defined by the following structure:

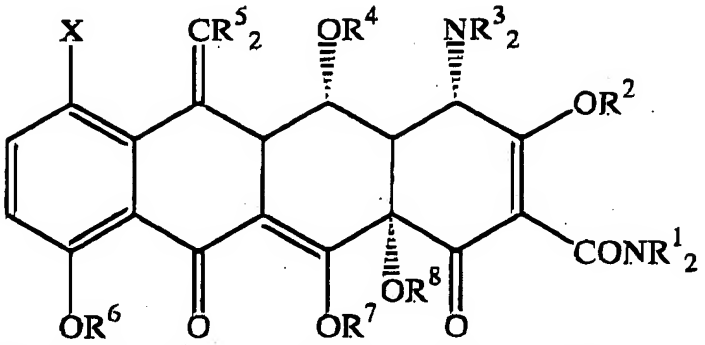


wherein R_1-R_5 may be a hydrogen atom, a halogen atom, a hydroxyl group, or any other organic composition comprising from 1-8 carbon atoms and optionally include a heteroatom such as nitrogen, oxygen, in linear, branched, or cyclic structural formats.

17. The method of claim 15 wherein the tetracycline is selected from the group consisting of compounds with the formula wherein R_1 and R_2 are hydrogen or a hydroxyl group; R_3 is hydrogen or a methyl group; R_4 is a hydrogen atom, a halogen, or a nitrogen containing entity and R_5 is a hydrogen atom, or nitrogen containing ring structure, compounds wherein the tetracycline is modified at any of positions 1 through 4 and 10 through 12, and compounds

wherein the tetracycline is modified by substitution of H at carbon 9 by a substituted amido group.

18. The method of claim 16 wherein the tetracycline has the following structure:



wherein R^1, R^2, R^3, R^4, R^5, R^6, R^7, and R^8 can be H, C1-C3 alkyl, phenyl, and aryl groups; and wherein X is an H, alkyl, alkoxy, phenoxy, aryloxy, amino group, amide, acyl, and halo group; and pharmaceutically acceptable salts thereof.

19. The method of claim 18 wherein the tetracycline is meclocycline, wherein R^1, R^2, R^4, R^5, R^6, R^7, and R^8 are H;

wherein R^3 is CH_3; and wherein X is a chloro group.

20. The method of claim 15 wherein the carrier for topical administration to the mucosa of the oral cavity and gastro-intestinal tract is selected from the group consisting of a mouthwash, lozenge, tablet, paste and gel.

21. The method of claim 15 wherein the carrier for topical administration comprises the tetracycline coated onto or encapsulated into a carrier selected from the group consisting of powders, pellets, microcapsules, liposomes, and emulsions, comprising suspending or dissolving the tetracycline and carrier in a liquid for adminstration of the tetracycline to the patient.

2. The method of claim 15 wherein the tetracycline is administered daily starting at least one day before the patient is treated with radiation or chemotherapy.

23. The method of claim 15 wherein the patient is treated between one and six times daily.